REMARKS

Applicant thanks the Examiner for his useful suggestions at the Interview of May 22, 2002. Applicant contacted the Examiner on May 23, 2002 regarding the Interview Summary. The Examiner stated that he had prepared the summary. However, Applicant has not yet received the summary.

At the interview, Applicant summarized the invention and presented possible claim amendments to overcome the rejections in the January 11th, 2002 Office Action. In particular, Applicant stated that melanocortin receptors MC1-R, MC2-R, MC3-R, MC4-R, and MC5-R were well known at the time of the invention and that these receptors were described in references incorporated by reference. The Examiner requested that a list of such receptors should be included in the specification.

The Applicant also stated that in Boston the physiological relevance of MC2-R in the adipocyte is unclear and no function is ascribed to the MC5-R receptor.

Amendment of the Specification.

The Applicant requests entry of an amendment to the paragraph beginning on page 68, line 24 of the specification to clarify that the genus of melanocortin receptors consists of the MC1-5 R receptors. No new matter has been added as a result of this amendment. Melanocortin receptors MC1-R through MC5-R are described in the specification on page 76, line 28. In addition, the cloning and characterization of each receptor is described in the specification on page 77, lines 1-13.

In the specification, the Applicant states that melanocortin receptor genes and proteins were well known (specification page 68, lines 24-27 to page 69, line 6).

Applicant has also incorporated by reference U.S. patent numbers 5,703,220 and 5,710,265 to Yamada et al.; U.S. patent number 5,532,347 to Cone et al.; and PCT publication WO 97/47316.and U.S. patent numbers 5,908,609 and 5,932,779 to Lee et al. as support. These references are attached and describe the family of five melanocortin receptors. For example, U.S. patent number 5,908,609 describes the five receptors MC1-R, MC2-R, MC3-R, MC4-R, and MC5-R (column 1, lines 29 -35). These receptors are also described in U.S. patent number 5,703,220 (column 5, lines 16-26) where the amino acid sequences of MC1-R (SEQ ID NO 2), MC2-R (SEQ ID NO 4), MC3-R (SEQ ID NO 6), MC4-R (SEQ ID NO 8) and MC5-R (SEQ ID NO 10) are also described.

Claim Amendments and New Claims.

Applicant requests entry of amended claims 19, 22, and 26-28, and new claims 30-38. No new matter had been added in the amendments or new claims.

Claim 19 has been amended to describe a test method for compounds that bind to a MC1-R, MC3-R, or MC5-R receptor. Support for this claim is found in the specification, page 60, lines 12-23 which describes a method of identifying compounds that regulate peripheral pathways of energy homeostasis including the step of contacting such a compound with an adipocyte. In addition, the specification, page 76, line 23 to page 77, line 18 describes methods of identifying compounds that selectively agonize or antagonize peripheral melanocortin receptors.

Claim 22 has been amended to include a listing of peripheral melanocortin receptors MC1-R, MC2-R, MC3-R, and MC5-R. Melanocortin receptors MC1-R through MC5-R are described in the specification on page 76, line 28. Support for this

listing is also found in the specification in the paragraph beginning on page 68, line 24 and ending on page 69, line 23. Here, the Applicant has also incorporated by reference U.S. patent numbers 5,703,220 and 5,710,265 to Yamada et al.; U.S. patent number 5,532,347 to Cone et al.; and PCT publication WO 97/47316 and U.S. patent numbers 5,908,609 and 5,932,779 to Lee et al. These references are attached and describe the family of five melanocortin receptors. For example, U.S. patent number 5,908,609 describes the five receptors MC1-R, MC2-R, MC3-R, MC4-R, and MC5-R (column 1, lines 29 -35). These receptors are also described in U.S. patent number 5,703,220 (column 5, lines 16-26) where the amino acid sequences of MC1-R (SEQ ID NO 2), MC2-R (SEQ ID NO 4), MC3-R (SEQ ID NO 6), MC4-R (SEQ ID NO 8) and MC5-R (SEQ ID NO 10) are also described. In addition, applicant has now amended this paragraph of the specification to clarify that the genus of melanocortin receptors consists of the MC1-5 R receptors. The cloning and characterization of each receptor is also described in the specification on page 77, lines 1-13.

The above references also describe peripheral melanocortin receptors. With the exception of MC4-R, which is a central nervous system receptor, all the melanocortin receptors are peripheral melanocortin receptors. For example, MC1-R is expressed in melanocytes (U.S. Patent 5,908,609, column 2, lines 15-17); MC2-R is expressed in the adrenal cortex (U.S. Patent 5,908,609, column 2, lines 15-17); MC3-R is expressed in gut tissues (U.S. Patent 5,710,265, column 5, lines 28-30) and MC5-R is expressed in lung, spleen and skeletal muscle (U.S. Patent 5,710,265, column 5, lines 33-36).

Claims 26-28 has been amended in the same manner as claim 22 to include a listing of peripheral melanocortin receptors MC1-R, MC2-R, MC3-R, and MC5-R. Support for these amendments is found in the same references cited for claim 22.

Claim 30 is directed to a method for identifying compounds that preferentially bind to and activate peripheral melanocortin receptors other than MC2-R. Melanocortin receptors MC1-R through MC5-R are described in the specification on page 76, line 28. Support for this claim is also found in the specification page 68, line 24 to page 60, line 22 which describes melanocortin receptors and incorporates references describing those receptors expressed at the periphery. In addition, an assay is described allowing the identification of compounds that preferentially activate one group of melanocortin receptors relative to another melanocortin receptor. An assay which discriminates between melanocortin receptors is also described in the specification on page 76, line 23 to page 77, line 18.

Claim 31 depends upon claim 30 and includes the additional limitation that the peripheral melanocortin receptor is MC3-R. Support for this claim is found in the specification page 68, line 24 to page 60, line 22 which describes melanocortin receptors and incorporates references describing those receptors, including MC3-R, expressed at the periphery. In addition, the specification, page 76, line 23 to page 77, line 18 describes methods of identifying compounds that selectively agonize or antagonize peripheral melanocortin receptors.

Claim 32 depends upon claim 30 and includes limitations on the method used to detect increases in receptor activity. These methods are found in original claim 3 and in the specification on page 71, lines 5-10.

Claim 33 depends upon claim 30 and limits the cell to a adipocyte and also includes limits on the method of detecting an increase in melanocortin receptor activity. These limitations are supported in original claim 4.

Claim 34 depends upon claim 30 and includes limitations on the method of detecting an increase in activity of the MC2-R melanocortin receptor. Such methods are described in original claim 5.

Claim 35 is directed to a method for identifying compounds that increase body weight by regulating peripheral pathways of energy homeostasis. The method includes the steps of contacting a cell which expresses a MC1-R, MC3-R or MC5-R receptor with a proopiomelanocortin (POMC) compound which binds to and activates the receptor and detecting whether the compound inhibits the receptor activity. Melanocortin receptors MC1-R through MC5-R are described in the specification on page 76, line 28. Support for this claim is also found in the specification page 68, line 24 to page 60, line 22 which describes melanocortin receptors and incorporates references describing those receptors expressed at the periphery. In addition, the specification, page 76, line 23 to page 77, line 18 describes methods of identifying compounds that <u>selectively</u> agonize or antagonize peripheral melanocortin receptors. Methods of engineering host cells to express one of the melanocortin receptors (MC1-R through MC5-R) are also described.

Claim 36 depends upon claim 35 and includes the additional limitation that the melanocortin receptor in MC3-R. Melanocortin receptors MC1-R through MC5-R are

described in the specification on page 76, line 28. Support for this claim is also found in the references cited in support of claim 35 and in the specification page 68, line 24 to page 60, line 22 which describes melanocortin receptors and incorporates references describing those receptors, including MC3-R, expressed at the periphery.

Claim 37 depends upon claim 35 and includes the additional limitation that the POMC compound is a melanocortin compound. Such compounds are described in the specification page 32, lines 24-27.

Claim 38 depends upon claim 35 and includes the additional limitation that the POMC compound is α-MSH, β-MSH, or γ-MSH. Such compounds are described in the specification page 21, lines 12-15.

Rejection of Claims 22-29 under 35 U.S.C. §112 first paragraph.

Claims 22-29 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time of the application was filed, had possession of the claimed invention. The Examiner alleges that although the specification discloses peripheral melanocortin receptors MC2 and MC5, the genus of peripheral melanocortin receptors encompassed by the claims is not disclosed.

Applicant traverses the Examiner's rejection. Melanocortin receptors MC1-R through MC5-R are described in the specification on page 76, line 28. In addition, the Applicant states that melanocortin receptor genes and proteins were well known (specification page 68, lines 24-27 to page 69, line 6). Applicant has also incorporated by

reference U.S. patent numbers 5,703,220 and 5,710,265 to Yamada et al.; U.S. patent number 5,532,347 to Cone et al.; and PCT publication WO 97/47316 and U.S. patent numbers 5,908,609 and 5,932,779 to Lee et al. as support. These references are attached and describe the family of five melanocortin receptors. For example, U.S. patent number 5,908,609 describes the five receptors MC1-R, MC2-R, MC3-R, MC4-R, and MC5-R (column 1, lines 29 -35). These receptors are also described in U.S. patent number 5,703,220 (column 5, lines 16-26) where the amino acid sequences of MC1-R (SEQ ID NO 2), MC2-R (SEQ ID NO 4), MC3-R (SEQ ID NO 6), MC4-R (SEQ ID NO 8) and MC5-R (SEQ ID NO 10) are also described. In addition, applicant has amended the specification to clarify that the genus of melanocortin receptors consists of the MC1-5 R receptors.

The above references also describe peripheral melanocortin receptors. With the exception of MC4-R, which is a central nervous system receptor, all the melanocortin receptors are peripheral melanocortin receptors. For example, MC1-R is expressed in melanocytes (U.S. Patent 5,908,609, column 2, lines 15-17); MC2-R is expressed in the adrenal cortex (U.S. Patent 5,908,609, column 2, lines 15-17); MC3-R is expressed in gut tissues (U.S. Patent 5,710,265, column 5, lines 28-30) and MC5-R is expressed in lung, spleen and skeletal muscle (U.S. Patent 5,710,265, column 5, lines 33-36).

In addition, methods of engineering host cells to express one of the melanocortin receptors (MC1-R through MC5-R) are also described in the specification page 77, lines 5-18.

Rejected claim 22 and dependent claims 23-25 are directed to a method for identifying compounds that preferentially bind to and activate peripheral melanocortin receptors but induce lesser activity by MC4-R receptors. Such a method is supported by the original specification on page 65 , lines 7-10, which describes a method which includes "selecting compounds which preferentially bind to/or activate peripheral melanocortin receptors as compared to central nervous system melanocortin receptors, and particularly, MC4-R". Applicant has amended claim 22 to include a listing of peripheral melanocortin receptors MC1-R, MC2-R, MC3-R, and MC5-R.

The Applicant has amended rejected claims 26-28 in the same manner as claim 22. These claims now also include a listing of peripheral melanocortin receptors MC1-R, MC2-R, MC3-R, and MC5-R.

The Examiner has also rejected claim 17 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. However, the reasons for the rejection indicate that this rejection is in fact directed to claims 22-29. The Examiner alleges that although the specification discloses peripheral melanocortin receptors MC2-R and MC5-R, it does not teach other peripheral melanocortin receptors expressed in peripheral tissues.

If the above rejection is directed to claims 22-29, Applicant traverses the Examiner's rejection. Melanocortin receptors MC1-R through MC5-R compose a well defined group of receptors and are described in the specification on page 76, line 28. In addition, the Applicant states that melanocortin receptor genes and proteins were well

known (specification page 68, lines 24-27 to page 69, line 6). Applicant has also incorporated by reference U.S. patent numbers 5,703,220 and 5,710,265 to Yamada et al.; U.S. patent number 5,532,347 to Cone et al.; and PCT publication WO 97/47316 and U.S. patent numbers 5,908,609 and 5,932,779 to Lee et al. as support. These references are attached and describe the family of five melanocortin receptors. For example, U.S. patent number 5,908,609 describes the five receptors MC1-R, MC2-R, MC3-R, MC4-R, and MC5-R (column 1, lines 29 -35). These receptors are also described in U.S. patent number 5,703,220 (column 5, lines 16-26) where the amino acid sequences of MC1-R (SEQ ID NO 2), MC2-R (SEQ ID NO 4), MC3-R (SEQ ID NO 6), MC4-R (SEQ ID NO 8) and MC5-R (SEQ ID NO 10) are also described. In addition, applicant has amended the specification to clarify that the genus of melanocortin receptors consists of the MC1-5 R receptors.

The above references also describe peripheral melanocortin receptors. With the exception of MC4-R, which is a central nervous system receptor, all the melanocortin receptors are peripheral melanocortin receptors. For example, MC1-R is expressed in melanocytes (U.S. Patent 5,908,609, column 2, lines 15-17); MC2-R is expressed in the adrenal cortex (U.S. Patent 5,908,609, column 2, lines 15-17); MC3-R is expressed in gut tissues (U.S. Patent 5,710,265, column 5, lines 28-30) and MC5-R is expressed in lung, spleen and skeletal muscle (U.S. Patent 5,710,265, column 5, lines 33-36).

In view of the above discussion, Applicant respectfully requests that the Examiner withdraw the rejection of claims 22-29 under 35 U.S.C. §112, first paragraph.

Rejection of Claims 6-9 and 17-21 under 35 U.S.C. §102(b).

Claims 6-9 and 17-21 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Boston *et al.* (1996). According to the Examiner, Boston *et al.* teach a method of pharmacological characterization of MC2 and MC5 receptors which are found in the peripheral tissue such as adipocytes. Allegedly, Boston *et al.* also teach that the adipocyte response to the melanocortin peptides results from the expression of both MC2 and MC5 receptors and also suggests that the MC2 receptor may also be involved in energy homeostasis.

Applicant asserts that the §102(b) based rejection is moot in view of the cancellation of claims 6-9 and 17-18 and 21, and the amendment of claim 19. However, to the extent the Examiner chooses to apply the rejection to the amended claims, it is respectfully traversed. Although Boston *et al.* teach the presence of MC2-R and MC5-R in adipose tissue, they state that the physiological relevance of MC5-R in the adipocyte is unclear and that no function is ascribed to the MC5-R receptor. In addition, Boston *et al.* only speculate as to the physiological role of MC2-R. Applicant has amended claim 19 and it is now directed to a method for identifying compounds that regulate peripheral pathways of energy homeostasis, including the step of detecting compounds that bind to a MC1-R, MC3-R, or MC5-R melanocortin receptor.

In view of the above discussion, Applicant respectfully requests that the Examiner withdraw the rejection of claims 19-20 under 35 U.S.C. §102(b).

Attached hereto is a marked up version of the changes made to the specification and claims. In reply to the Office Action dated January 11th, 2002, favorable

reconsideration and allowance of this application are respectively requested for the reasons set forth in the above remarks. If, for any reason, the Examiner is unable to allow the application on the next Office Action and feels that an interview would be helpful to resolve any remaining issues, he is respectfully requested to contact the undersigned attorney at (312) 321-4229.

Respectfully submitted,

Dated: June 28th, 2002.

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VERSION WITH MARKINGS TO SHOW CHANGES MADE.

IN THE SPECIFICATION

It is noted that melanocortin receptor genes and proteins, and *in vitro* assays for determining melanocortin receptor activity are well known in the art. For example, U.S. Patent Nos. 5,703,220 and 5,710,265 to Yamada et al.; U.S. Patent No. 5,532,347 to Cone et al.; and PCT Publication WO 97/47316 and U.S. Patent Nos. 5,908,609 and 5,932,779 to Lee et al.; describe known melanocortin receptors MC1-R, MC2-R, MC3-R, MC4-R, and MC5-R and genes encoding such receptors, [including MC2-R, MC4-R and MC5-R,] as well as *in vitro* and *in vivo* assays for identifying compounds which bind to and/or activate such receptors. Each of these patents and PCT publication is incorporated herein by reference in its entirety, and particularly, with regard to disclosed methods for evaluating the activity of melanocortin receptors and the identification of compounds which bind to such receptors. However, none of the above-referenced patents or PCT publication discloses a method for identifying compounds useful for regulating body weight by identifying compounds which bind to, activate or inhibit activity of peripheral melanocortin receptors, and particularly, which preferentially bind to, activate or inhibit activity over central melanocortin receptors. Indeed, it is particularly noted that although the patents and PCT publication of Lee et al. are directed to identifying compounds for regulation of body weight, the target receptor of Lee et al. (i.e., MC4-R) is *directly opposite* of the target receptors of the present invention (i.e. MC2-R and/or MC5-R), since the methods of Lee et al. target the central mechanisms of energy homeostasis (e.g., appetite), while the present invention targets the peripheral mechanisms of energy homeostasis (e.g., lipolysis and/or free fatty acid uptake). Prior to the present invention,

it was not known that the peripheral melanocortin receptors (and not central melanocortin receptors) and the compounds that bind to such receptors regulate metabolic efficiency. Moreover, the present inventors are the first to disclose an assay for the identification of compounds that preferentially bind to, activate, or inhibit the activity of MC2-R and/or MC5-R as compared to MC4-R, or which bind to, activate, or inhibit the activity of MC2-R and/or MC5-R in the absence of significant MC4-R binding or activation.

IN THE CLAIMS

1. (Allowed) A method for identifying compounds that regulate body weight by preferentially regulating peripheral pathways of energy homeostasis, comprising:

a. contacting a putative regulatory compound with a cell which expresses a melanocortin receptor selected from the group consisting of melanocortin 2-receptor (MC2-R) and melanocortin 5-receptor (MC5-R);

b. detecting whether the putative regulatory compound increases said melanocortin receptor activity;

c. contacting said putative regulatory compound with a cell which expresses a melanocortin 4-receptor (MC4-R); and,

d. detecting whether the putative regulatory compound increases MC4-R activity;

wherein putative regulatory compounds that induce greater MC2-R activity or MC5-R activity as compared to MC4-R activity are identified as compounds that regulate body weight by preferentially regulating peripheral pathways of energy homeostasis.

2. (Allowed) The method of Claim 1, wherein said melanocortin receptor of (a) and (b) is MC2-R.

3. (Allowed) The method of Claim 1, wherein said step (b) of detecting is selected from the group consisting of measurement of melanocortin receptor transcription, measurement of melanocortin receptor translation, measurement of phosphorylation of melanocortin receptor, measurement of melanocortin receptor ligand

binding activity, measurement of G protein activation, and measurement of melanocortin receptor translocation within a cell.

4. (Allowed) The method of Claim 1, wherein said cell of step (a) is an adipocyte, and wherein step (b) of detecting is selecting from the group consisting of measurement of melanocortin receptor transcription, measurement of melanocortin receptor translation, measurement of G protein activation, measurement of melanocortin receptor ligand binding activity, measurement of melanocortin receptor translocation within a cell, measurement of lipolysis by said cell and measurement of free fatty acid uptake by said cell.

5. (Allowed) The method of Claim 1, wherein said step (d) of detecting is selected from the group consisting of measurement of MC4-R transcription, measurement of MC4-R translation, measurement of phosphorylation of MC4-R, measurement of MC4-R ligand binding activity, and measurement of MC4-R translocation within a cell.

15. (Allowed) A method for identifying compounds that regulate body weight by regulating peripheral pathways of energy homeostasis, comprising:

a. contacting a putative regulatory compound with a cell or cell lysate containing a reporter gene operatively associated with a regulatory element of a melanocortin receptor selected from the group consisting of melanocortin 2-receptor (MC2-R) and melanocortin 5-receptor (MC5-R);

b. detecting expression of the reporter gene product;

c. contacting a putative regulatory compound with a cell or cell lysate containing a reporter gene operatively associated with a regulatory element of a melanocortin 4-receptor (MC4-R); and

d. detecting expression of the reporter gene product;

wherein putative regulatory compounds that increase expression of the reporter gene product of (b) as compared to the reporter gene product of (d) are identified as compounds that regulate body weight by preferentially regulating peripheral pathways of energy homeostasis.

16. (Allowed) The method of Claim 15, wherein said melanocortin receptor is MC2-R.

19. (Twice Amended) A method for identifying compounds that regulate peripheral pathways of energy homeostasis, comprising:

a. contacting a putative regulatory compound with an isolated adipocyte; and,

b. detecting putative regulatory compounds that bind to a melanocortin receptor on said adipocyte, <u>wherein said melanocortin receptor is a MC1-R, MC3-R, or MC5-R receptor, and</u> wherein putative regulatory compounds that bind to <u>said</u> melanocortin [receptors] <u>receptor</u> on said adipocytes are identified as compounds that regulate body weight by regulating peripheral pathways of energy homeostasis.

20. The method of Claim 19, wherein said step of detecting further comprises detecting putative regulatory compounds which produce a result selected from the group consisting of stimulation of lipolysis in said adipocytes and inhibition of the uptake of fatty acids by said adipocytes, wherein putative regulatory compounds that bind to melanocortin receptors on said adipocytes that produce said result are identified as compounds that regulate body weight by regulating peripheral pathways of energy homeostasis.

22. (Amended) A method for identifying compounds that preferentially bind to and activate peripheral melanocortin receptors comprising:

a. contacting a putative regulatory compound with a cell which expresses a peripheral melanocortin receptor selected from a group consisting of MC1-R, MC2-R, MC3-R and MC5-R [that is expressed in the peripheral tissues];

b. detecting whether the putative regulatory compound increases activity of said melanocortin receptor;

c. contacting said putative regulatory compound with a cell which expresses a melanocortin 4-receptor (MC4-R); and

d. detecting whether the putative regulatory compound increases MC4-R activity;

wherein putative regulatory compounds that induce greater activity by said peripheral melanocortin receptor [that is expressed in the periphery] as compared to said MC4-R are identified as compounds that preferentially bind to and activate peripheral melanocortin receptors.

23. The method of Claim 22, wherein said step (b) of detecting is selected from the group consisting of measurement of melanocortin receptor transcription, measurement of melanocortin receptor translation, measurement of phosphorylation of melanocortin receptor, measurement of melanocortin receptor ligand binding activity, measurement of G protein activation, and measurement of melanocortin receptor translocation within a cell.

24. The method of Claim 22, wherein said cell of step (a) is an adipocyte, and wherein said step (b) of detecting is selected from the group consisting of measurement of melanocortin receptor transcription, measurement of melanocortin receptor translation, measurement of phosphorylation of melanocortin receptor, measurement of G protein activation, measurement of melanocortin receptor ligand binding activity, measurement of melanocortin receptor translocation within a cell, measurement of lipolysis by said cell and measurement of free fatty acid uptake by said cell.

25. The method of Claim 22, wherein said step (d) of detecting is selected from the group consisting of measurement of MC4-R transcription, measurement of MC4-R translation, measurement of phosphorylation of MC4-R, measurement of MC4-R ligand binding activity, and measurement of MC4-R translocation within a cell.

26. (Amended) A method for identifying compounds that preferentially bind to and activate peripheral melanocortin receptors, comprising:

a. contacting a putative regulatory compound with a cell or cell lysate containing a reporter gene operatively associated with a regulatory element of a peripheral melanocortin receptor selected from a group consisting of MC1-R, MC2-R, MC3-R and MC5-R [that is expressed in the periphery];

b. detecting expression of the reporter gene product;

c. contacting a putative regulatory compound with a cell or cell lysate containing a reporter gene operatively associated with a regulatory element of a melanocortin 4-receptor (MC4-R); and,

d. detecting expression of the reporter gene product;

wherein putative regulatory compounds that increase expression of the reporter gene product of (b) as compared to the reporter gene product of (d) are identified as compounds that preferentially bind to and activate peripheral melanocortin receptors.

27. (Amended) A method for identifying compounds for increasing body weight by inhibition of peripheral melanocortin receptors, comprising:

a. contacting a putative regulatory compound with a cell or cell lysate containing transcripts of a peripheral melanocortin receptor selected from a group consisting of MC1-R, MC2-R, MC3-R and MC5-R [that is expressed in the periphery]; and,

b. detecting translational inhibition of the melanocortin receptor transcript;

wherein putative regulatory compounds that inhibit said melanocortin receptor transcript are identified as compounds that inhibit peripheral melanocortin receptor expression.

28. (Amended) A method for identifying compounds that regulate peripheral melanocortin receptors selected from a group consisting of MC1-R, MC2-R, MC3-R and MC5-R, comprising:

a. contacting a putative regulatory compound with an isolated adipocyte; and,

b. detecting putative regulatory compounds that bind to a melanocortin receptor on said adipocyte, wherein putative regulatory compounds that bind to melanocortin receptors on said adipocytes are identified as compounds that regulate peripheral melanocortin receptors.

29. (Amended) The method of Claim 28, wherein said step of detecting further comprises detecting putative regulatory compounds which produce a result selected from the group consisting of stimulation of lipolysis in said adipocytes and inhibition of the uptake of fatty acids by said adipocytes, wherein putative regulatory compounds that bind to melanocortin receptors on said adipocytes and that produce said result are identified as compounds that regulate peripheral melanocortin receptors.

30. (New) A method for identifying compounds that preferentially bind to and activate peripheral melanocortin receptors other than MC2-R comprising:

a. contacting a putative regulatory compound with a cell which expresses a peripheral melanocortin receptor selected from a group consisting of MC1-R, MC3-R and MC5-R;

b. detecting whether the putative regulatory compound increases activity of said melanocortin receptor;

c. contacting said putative regulatory compound with a cell which expresses a melanocortin 2-receptor (MC2-R); and,

d. detecting whether the putative regulatory compound increases activity of said MC2-R melanocortin receptor;

wherein putative regulatory compounds that induce greater activity by said peripheral melanocortin receptor as compared to said MC2-R are identified as compounds that preferentially activate peripheral melanocortin receptors other than MC2-R.

31. (New) The method of Claim 30, wherein said peripheral melanocortin receptor is MC3-R.

32. (New) The method of Claim 30, wherein said step (b) of detecting is selected from the group consisting of measurement of melanocortin receptor transcription, measurement of melanocortin receptor translation, measurement of phosphorylation of melanocortin receptor, measurement of melanocortin receptor ligand binding activity, measurement of G protein activation, and measurement of melanocortin receptor translocation within a cell.

33. (New) The method of Claim 30, wherein said cell of step (a) is an adipocyte, and wherein step (b) of detecting is selecting from the group consisting of measurement of melanocortin receptor transcription, measurement of melanocortin receptor translation, measurement of G protein activation, measurement of melanocortin receptor ligand binding activity, measurement of melanocortin receptor translocation within a cell, measurement of lipolysis by said cell and measurement of free fatty acid uptake by said cell.

34. (New) The method of Claim 30, wherein said step (d) of detecting is selected from the group consisting of measurement of MC2-R transcription, measurement of MC2-R translation, measurement of phosphorylation of MC2-R, measurement of MC2-R ligand binding activity, and measurement of MC2-R translocation within a cell.

35. (New) A method for identifying compounds that increase body weight by regulating peripheral pathways of energy homeostasis, comprising:

a. contacting a cell which expresses a melanocortin receptor selected from the group consisting of MC1-R, MC3-R and MC5-R with proopiomelanocortin (POMC) compound which binds to and activates said melanocortin receptor in the presence and absence of a putative regulatory compound;

b. detecting whether said putative regulatory compound inhibits said melanocortin receptor activity;

wherein putative regulatory compounds that inhibit said melanocortin receptor activity are identified as compounds that increase body weight by regulating peripheral pathways of energy homeostasis.

36. (New) The method of Claim 35, wherein said melanocortin receptor is MC3-R.

37. (New) The methods of Claim 35, wherein said POMC compound is a melanocortin compound.

38. (New) The method of Claim 35, wherein said POMC compound is selected from the group of α-MSH, β-MSH and γ-MSH.